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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,652	03/11/2004	Yongjun Guo	3882-P03136US01	6508

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DANN, DORFMAN, HERRELL & SKILLMAN
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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,652	GUO, YONGJUN	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *6-24 and 29-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,25-28 and 33* is/are rejected.

7)☒ Claim(s) *2, 25-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/07/2007 has been entered.

2. Claims 1-33 are pending. Claim 34 has been cancelled. Claims 6-24, and 29-32 have been withdrawn.

3. Rejections are reiterated or newly applied to Claims 1-5, 25-28, and 33. This action is NONFINAL

Claim Objections

4. As stated in MPEP 608.01(n), "The test as to whether a claim is a proper dependent claim is that it shall include every limitation of the claim from which it depends (35 U.S.C. 112, fourth paragraph) or in other words that it shall not conceivably be infringed by anything which would not also infringe the basic claim... On the other hand, if claim 1 recites a method of making a specified product, a claim to the product set forth in claim 1 would not be a proper dependent claim since it is conceivable that the product claim can be infringed without infringing the base method claim if the

product can be made by a method other than that recited in the base method claim." In the present situation claim 2 is improper because it only refers to the sequence of claim 1 whereas claim 1 is drawn to a nucleic acid. Claims 25-28 are improperly depended because these claims are referring to SEQ ID No. 1 of Claim 1 and not to the nucleic acid molecule comprising SEQ ID NO. 1 as recited in Claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25-28 are indefinite over the phrase "anneals specifically with a target portion" in Claim 25 line 4. It is unclear the metes and bounds of the phrase "anneals specifically with a target portion". The phrase is not defined in the specification, therefore it is unclear if "specifically anneals" means that the probe only anneals to the stated nucleic acid or if it may also anneal to other nucleic acids under certain, unspecified conditions.

Claim Rejections - 35 USC § 112/Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

A kit for identifying a polymorphism at position 69 of SEQ ID No. 1 wherein the nucleotide at position 69 is a "C" or a "T", comprising a) a first oligonucleotide probe selected from the group consisting of SEQ ID No. 6 and 7 wherein there is a fluorescent label and fluorescence quencher attached to SEQ ID No. 6 and 7 and b) a pair of primers consisting of SEQ ID NO. 4 and 5,

does not reasonably provide enablement for identifying ANY polymorphisms in SEQ ID NO. 1.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the claims

The claims are drawn to a kit for identifying ANY polymorphism in SEQ ID No. 1

of Claim 1 comprising a probe selected from the group consisting of SEQ ID No. 6 and 7 and primers consisting of SEQ ID No. 4 and 5.

The claim encompasses identification of ANY polymorphism in SEQ ID NO. 1, however, the specification only teaches a kit for the identification of position 69 in SEQ ID NO. 1 wherein there is a "C" or a "T" at position 69 in SEQ ID NO. 1. As discussed below, the instant specification does not support a kit for the identification of ANY polymorphism of SEQ ID No. 1.

Nature of the Invention

The claims are broadly drawn to a kit for identifying any polymorphism in SEQ ID No. 1. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Teachings in the Specification and Working Examples

The specification discloses SEQ ID No. 6 and 7 (p. 24 lines 30-35), which can be placed in a kit. SEQ ID No. 6 is a 100% match over a region of SEQ ID NO. 1 except at position 69 SEQ ID NO. 6 has an "A" and at position 69 SEQ ID NO. 7 has an "G". Therefore, the probe of SEQ ID NO. 6 will hybridize to SEQ ID NO. 1 when the sequence has a "T" at position 69. The probe of SEQ ID NO. 7 will hybridize to SEQ ID NO. 1 when the sequence has a "C" at position 69. Though the specification has

shown that these probes can detect a mutation at position 69 of SEQ ID NO. 1, it is unpredictable that these probes can identify other polymorphisms in SEQ ID No. 1.

It is unpredictable that probes, which hybridize to a specific region and differ at one location (position 69) would be able to identify any polymorphism at any location in SEQ ID No. 1. Therefore, the specification has not provided clear examples to correlate the identification of ANY polymorphism with the hybridization of SEQ ID NO. 6 or 7 with the sequence of SEQ ID No. 1.

Amount of Direction or Guidance Provided by the Specification

The specification does not provide any specific guidance as to how to identify any polymorphism in SEQ ID NO. 1 with the hybridization of SEQ ID No. 6 or 7. The specification only discloses kits comprising SEQ ID No. 6 or 7, which identify a "C" or a "T" at position 69 in SEQ ID NO. 1. The specification does not provide support for the identification of any polymorphism in SEQ ID No. 1 by hybridization of SEQ ID NO. 6 or 7.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there are a significant number of parameters, which would have to be studied prior to being able to practice the claimed invention as broadly as written. The skilled artisan would have to determine identification of ANY polymorphisms in SEQ ID No. 1 using probes (SEQ ID NO. 6 and 7) which hybridize only to a specific location in SEQ ID NO. 1 and which differ only at position 69.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the instant case, the specification does not provide any predictable identification of ANY polymorphism in SEQ ID No. 1 using probes consisting of SEQ ID NO. 6 and 7. The specification only discloses an example of detection a "C" or a "T" at position 69 using the kit comprising a probe consisting of SEQ ID No. 6 or 7. Therefore the specification has not established that the presently claimed kit can be used to identify any polymorphism in SEQ ID No. 1.

Accordingly the lack of disclosure in the specification, it would require undue experimentation for one of skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112-Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 25-28, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an isolated nucleic acid molecule comprising the sequence of SEQ ID No. 1. Claim 2 is drawn to an isolated nucleic acid molecule comprising a sequence fully complementary complementary to the sequence of SEQ ID No. 1. Claims 3-4 are drawn to a vector wherein the reporter gene sequence encodes luciferase. Claim 5 is drawn to a host cell. Claim 25 is drawn to a kit comprising a first oligonucleotide probe which anneals specifically with a target portion of the mammal's genome, wherein said first probe comprises a first fluorescent label and a first fluorescence quencher attached to separate nucleotide residues thereof and said target portion includes the nucleotide residue located at position 69 of SEQ ID No. 1 and a pair of primers for amplifying a reference portion of the FGF-3 gene wherein said reference portion includes the nucleotide residue located at position 69 of SEQ ID No. 1. Claim 26 is drawn to a kit including DNA polymerase having 5' to 3' exonuclease activity. Claim 27 is drawn to a kit further comprising a second oligonucleotide probe, wherein said first probe is completely complementary to said target portion if the nucleotide

residue located at position 69 of SEQ ID No. 1 is cytosine and said second oligonucleotide probe is completely complementary to said target portion if the nucleotide residue located at position 69 of SEQ ID No. 1 is thymine. Claim 28 is drawn to a kit further including an instructional material. Claim 33 is drawn to a microarray having at least one oligonucleotide probe that can anneal with a target portion of a mammal's genome, wherein the target portion includes the nucleotide residue located at position 69 of SEQ ID No. 1.

The claims do not describe the number or identity of nucleotides flanking the recited nucleic acid fragment of SEQ ID No. 1. The claims encompass nucleic acids, which comprise any nucleic acid variant of any size, fragments of SEQ ID No. 1, and sequence, which are complementary to SEQ ID No. 1 for any number of nucleotides. The claims encompass variants, which include nucleotide substitutions, additions, deletions, translocations, and truncations. Claims encompass any number of sequences, which must include only the cytosine of position 69 of SEQ ID No. 1. The specification does not describe the sequences encompassed by "fully complementary to SEQ ID No. 1"

The claims also encompass a large genus of sequences from any mammal. The specification does not describe SEQ ID no. 1 in any mammalian species other than human.

The specification does not teach the percent structural identity needed for a sequence to be considered FGF3. The specification also does not indicate how much variation a sequence may have; therefore, the claims with regard to the "target" sequences can be any number of variations, mutations, or homologs.

The genus of the claimed nucleic acids molecules encompasses substantial variability among the species of nucleic acids, but only a few mutations have been

described. The genus of the claimed invention encompasses a large variable genus of mutants, variants, and homologs from any source.

With regard to Claim 33, the claim does not define any of the additional probes that may be included in terms of a structure therefore in view of the language "at least one probe" the specification has not described all the possible species, which would be encompassed by the broad claim language.

With regard to Claim 25-26 the claim does not define the nucleotide identity or location of the polymorphism. The specification has not adequately described enough species to encompass the broad claim languages as any variant at any location in SEQ ID NO. 1. The specification only describes one nucleotide location (i.e. position 69).

With regard to Claims 27 and 28, the structure for the second probe is not provided therefore the probe can be comprised as any number of nucleotides complementary to the target portion.

Further, Claims 25-28 also has the same issues concerning the flanking sequences of SEQ ID NO. 1 as presented above. Therefore, the specification has not clearly described the structure of the genus of potential sequences encompassed by the broad claim language.

The specification fails to sufficiently describe the claimed invention in clear and exact terms so that a skilled artisan would recognize that the applicants were in possession of the claimed invention at the time of filing.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding

genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids and mammalian species in view of the species disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The sequences encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly diverse. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

The reply traverses the rejection. The reply asserts that the specification describe sequences flanking SEQ ID NO. 1 by the description of the luciferase gene (p. 8 2nd paragraph). The reply asserts that sequence that flank SEQ ID No 1 can be any sequence and that its standard practice for the USPTO to determine claims drawn to isolated nucleic acids comprising novel genes satisfy written description (p. 8 last full paragraph). The reply asserts that since claim 1 has not been rejected under 35 USC 102 then there is no other sequences known that comprise SEQ ID No. 1.

Though, the specification provides support an isolated nucleic acid molecule consisting of the sequence of SEQ ID No. 1 and a vector comprising the isolated nucleic acid molecule of claim 1, operable linked to a reporter gene wherein the reporter gene

sequence encodes a luciferase, the specification does not provide support for ANY flanking sequence around SEQ ID No. 1. Therefore, though the specification provides one specific example it does not adequately provide support for the large genus of any potential nucleotides flanking SEQ ID No. 1.

The instantly claimed sequence (SEQ ID No. 1) comprising only 564 base pairs, therefore the claims are not drawn to a complete gene wherein the open reading frames are known. Therefore, it is unclear which nucleotides flanking the claimed SEQ ID NO. 1 would have the same functionality as SEQ ID No. 1.

Though SEQ ID No. 1 is newly rejected under 35 USC 102(a) as presented below, the rejection of the claim under 35 USC 102 is not predictive of adequate disclosure in the specification to overcome a 35 USC 112/Written Description rejection. The specification still has not provided support for the broadly claimed genus of nucleotides possible with the broad claim language. Therefore, there is not adequate support in the specification or the art as to which sequences would be in the genus and would maintain the functionality of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Wang et al. (US Patent Application Publication 2002/0198371 December 26, 2002).

With regard to Claim 1, Wang et al teaches an isolated nucleic acid molecule comprising SEQ ID No. 1 (nucleotides 107-670 of SEQ ID No. 142127 of Wang et al.). It is noted that position 69 of the instant SEQ ID No. 1 is an "N" which would encompass the "C" at position 175 of SEQ ID NO. 142127. It is noted that position 176 of SEQ ID No. 142127 is a "K" which would encompass the "G" at position 70 of SEQ ID NO. 1 (see alignment below wherein the instant SEQ ID No. 1 is "Qy" and SEQ ID No. 142127 is "Db").

```
Qy          1 GCAGCCCTGCCTCAGAAAACAGAAGGACGCAGCACACTCACGGTGACTCACCCCCATGTG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        107 GCAGCCCTGCCTCAGAAAACAGAAGGACGCAGCACACTCACGGTGACTCACCCCCATGTG 166

Qy         61 GCTGGAGGNGAGGGAGCCTCCTGAGGCAGGGCCAGGGCAGCCGTCAGGTGGGTGACGGCA 120
              |||||||| :|||||||||||||||||||||||||||||||||||||||||||||||||||
Db        167 GCTGGAGGCKAGGGAGCCTCCTGAGGCAGGGCCAGGGCAGCCGTCAGGTGGGTGACGGCA 226

Qy        121 GGGGTCTTGCCATGGTGGGCACAGGGGCTGCATACAGCTTACTCAGTGACAATCGAGTCC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        227 GGGGTCTTGCCATGGTGGGCACAGGGGCTGCATACAGCTTACTCAGTGACAATCGAGTCC 286

Qy        181 CTGGTGCCAGCCTCTGGAAGTCTGGAAGTGAGCAATGTTTCCCATTAAGGAAAGTGTGTG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        287 CTGGTGCCAGCCTCTGGAAGTCTGGAAGTGAGCAATGTTTCCCATTAAGGAAAGTGTGTG 346

Qy        241 GCCGGCCATGCCCCCCAACGTTGCACACTCACTGCCTTTGCAGGGTTGGGGCTTCCAGTC 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        347 GCCGGCCATGCCCCCCAACGTTGCACACTCACTGCCTTTGCAGGGTTGGGGCTTCCAGTC 406

Qy        301 ACAGGGTCCCATCCACGTACCAGCCCAGGTGGCTGCAGAAGGTCCCTCGCAGTCATGAAA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        407 ACAGGGTCCCATCCACGTACCAGCCCAGGTGGCTGCAGAAGGTCCCTCGCAGTCATGAAA 466

Qy        361 CCAAGGGAGGCTTGGGAAACCACATCTGAAGGGCATGGCTTTGATTTAGTGAGAGGGTGG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        467 CCAAGGGAGGCTTGGGAAACCACATCTGAAGGGCATGGCTTTGATTTAGTGAGAGGGTGG 526

Qy        421 GGCTGGGCTGGGCAAGGCCACCAGGTCTGAGTCAGAGCCAGAGGCAGGAAGCTGGTCCCC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        527 GGCTGGGCTGGGCAAGGCCACCAGGTCTGAGTCAGAGCCAGAGGCAGGAAGCTGGTCCCC 586

Qy        481 AGCACTGCCCGCCGCCTCTGCGATGCAGTCCTCCTGGCCACCTGAGAACAGCCTGTAGAG 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        587 AGCACTGCCCGCCGCCTCTGCGATGCAGTCCTCCTGGCCACCTGAGAACAGCCTGTAGAG 646

Qy        541 AGGCAGTGGCGTCTTTCGGACTTC 564
              ||||||||||||||||||||||||
Db        647 AGGCAGTGGCGTCTTTCGGACTTC 670
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With regard to Claim 2, Wang et al teaches a complement of SEQ ID NO. 1 (nucleotides 107-670 of SEQ ID No. 142127 of Wang et al.).

With regard to Claims 3 and 5, Wang et al. teaches a vector in a host cell (E. coli) (p. 4 paragraph 34).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 25, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (US Patent Application Publication 2002/0198371 December 26, 2002) in further view of Hogan et al. (US Patent 5541308 July 30, 1996).

Wang et al teaches an isolated nucleic acid molecule comprising SEQ ID No. 1 (nucleotides 107-670 of SEQ ID No. 142127 of Wang et al.). It is noted that position 69 of the instant SEQ ID No. 1 is an "N" which would encompass the "C" at position 175 of SEQ ID NO. 142127. It is noted that position 176 of SEQ ID No. 142127 is a "K" which would encompass the "G" at position 70 of SEQ ID NO. 1 (see alignment below wherein the instant SEQ ID No. 1 is "Qy" and SEQ ID No. 142127 is "Db").

```
Qy        1 GCAGCCCTGCCTCAGAAAACAGAAGGACGCAGCACACTCACGGTGACTCACCCCCATGTG 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      107 GCAGCCCTGCCTCAGAAAACAGAAGGACGCAGCACACTCACGGTGACTCACCCCCATGTG 166

Qy       61 GCTGGAGGNGAGGGAGCCTCCTGAGGCAGGGCCAGGGCAGCCGTCAGGTGGGTGACGGCA 120
            |||||||| :||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      167 GCTGGAGGCKAGGGAGCCTCCTGAGGCAGGGCCAGGGCAGCCGTCAGGTGGGTGACGGCA 226

Qy      121 GGGGTCTTGCCATGGTGGGCACAGGGGCTGCATACAGCTTACTCAGTGACAATCGAGTCC 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      227 GGGGTCTTGCCATGGTGGGCACAGGGGCTGCATACAGCTTACTCAGTGACAATCGAGTCC 286

Qy      181 CTGGTGCCAGCCTCTGGAAGTCTGGAAGTGAGCAATGTTTCCCATTAAGGAAAGTGTGTG 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      287 CTGGTGCCAGCCTCTGGAAGTCTGGAAGTGAGCAATGTTTCCCATTAAGGAAAGTGTGTG 346

Qy      241 GCCGGCCATGCCCCCCAACGTTGCACACTCACTGCCTTTGCAGGGTTGGGGCTTCCAGTC 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      347 GCCGGCCATGCCCCCCAACGTTGCACACTCACTGCCTTTGCAGGGTTGGGGCTTCCAGTC 406

Qy      301 ACAGGGTCCCATCCACGTACCAGCCCAGGTGGCTGCAGAAGGTCCCTCGCAGTCATGAAA 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      407 ACAGGGTCCCATCCACGTACCAGCCCAGGTGGCTGCAGAAGGTCCCTCGCAGTCATGAAA 466

Qy      361 CCAAGGGAGGCTTGGGAAACCACATCTGAAGGGCATGGCTTTGATTTAGTGAGAGGGTGG 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      467 CCAAGGGAGGCTTGGGAAACCACATCTGAAGGGCATGGCTTTGATTTAGTGAGAGGGTGG 526

Qy      421 GGCTGGGCTGGGCAAGGCCACCAGGTCTGAGTCAGAGCCAGAGGCAGGAAGCTGGTCCCC 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      527 GGCTGGGCTGGGCAAGGCCACCAGGTCTGAGTCAGAGCCAGAGGCAGGAAGCTGGTCCCC 586

Qy      481 AGCACTGCCCGCCGCCTCTGCGATGCAGTCCTCCTGGCCACCTGAGAACAGCCTGTAGAG 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      587 AGCACTGCCCGCCGCCTCTGCGATGCAGTCCTCCTGGCCACCTGAGAACAGCCTGTAGAG 646

Qy      541 AGGCAGTGGCGTCTTTCGGACTTC 564
            ||||||||||||||||||||||||
Db      647 AGGCAGTGGCGTCTTTCGGACTTC 670
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Therefore Wang et al. teaches nucleotide variability in the region of the target where SEQ ID NO. 6 and 7 anneal (e.g. position 175 of SEQ ID NO. 142127 is a variable region).

With regard to Claim 25, Wang et al. teaches oligonucleotide primers were chose according to parameters that generated PCR products which amplify the locus in which a SNP is detectable (p. 3 paragraph 30 and p. 4 paragraph 39). Though Wang et al. does not specifically teach primers SEQ ID NO. 4 and 5, Wang et al. does suggest making primers to produce a fragment of target, which comprises a SNP region. This fragment (SEQ ID no. 142127) would comprise the nucleotides, which are identical to the instant claims SEQ ID No. 1.

Wang et al. teaches SNP probes which are complementary to a SNP nucleic acid (p. 2 paragraph 21). Wang et al. teaches the probes are 15 to 25 nucleotides in length and have a fluorescent label (p. 2 paragraph 21). Wang et al. teaches a polymorphic region is in SEQ ID no. 142127 at position 175 (position 70 of SEQ ID NO. 1). Therefore Wang et al. teaches probes which anneal to the same location as SEQ ID No. 6 and 7. Wang et al. teaches that these probes are complementary to the SNP nucleic acid, therefore; therefore probes would have a "C" at position 174 of SEQ ID No. 142127 (position 69 of SEQ ID NO. 1). Therefore Wang et al. teaches probes which would hybridize to the same region as SEQ ID No. 6 and 7 of SEQ ID No. 1.

With regard to Claim 27, Wang et al. teaches a probe which would be completely complementary to the target sequence at position 69 if it was a "C". Wang et al.

teaches that these probes are complementary to the SNP nucleic acid, therefore; therefore probes would have a "C" at position 174 of SEQ ID No. 142127 (position 69 of SEQ ID NO. 1).

With regard to Claim 28, the limitation that the kit contains instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004) (holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

However, Wang et al. does not teach the specific SEQ ID Nos of 4-7 to identify a polymorphism.

Hogan teaches guidance for the selection of primers and probes. Hogan et al. teaches the use of specific primers and probes to amplify the 16S region of bacteria. Hogan et al. provides guidance for the selection of probes.

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> Fist, probes should be positioned so as to minimize the stability of the probe: nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarily to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe: target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G: C base

> pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10 °C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structure inhibitory to hybridization are less preferred. Finally probes with extensive self complementarity should be avoided." (See Column 6 lines 66-67 and Column 7 lines 1-29).

Hogan et al. teaches, "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (see Column 10, lines 13-15). Therefore Hogan et al. teaches taking a sequence and fragmenting the sequence into smaller oligonucleotides to be used as probes. Hogan et al. teaches that these probes are preferable to be between about 15 and about 50 bases in length.

Though, Hogan et al. does not specifically teach the SEQ ID Nos 4-6, he does suggest the fragmentation of a larger fragment (i.e. the target sequence) into smaller oligonucleotide probes.

Therefore, the ordinary artisan would have been motivated to select any number of oligonucleotide fragments from the target sequence including SEQ ID Nos 4-6 which would amplify the SNP targeted region and hybridize to the SNP region (i.e. in the case of Wang et al. position 70 of SEQ ID No. 1). The art of designing probes (oligonucleotides) at the time the invention was made was very well described in the art. The art uses alignment programs to align sequences of interest and then uses algorithms to select and test probes and primers for their desired function of either detecting or distinguishing particular organisms. Designing probes that are equivalents

to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan et al. Moreover there are many Internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes. The claimed probes are prima facie obvious over the cited references in the absence of secondary considerations, given the extensive teachings in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the SNP targeted region as taught by Wang et al. to design primers to amplify the targeted region (comprising SEQ ID NO. 1) and probes to identify the SNPs. The skilled artisan would use the design constraints of probes taught by Hogan et al. to obtain equivalent alternative probes of the claimed invention. The ordinary artisan would be motivated to have designed and test new probes to obtain additional oligonucleotides that function to identify SNP regions and identify oligonucleotides with improved properties.

Conclusion

11. No Claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Katherine Salmon
Examiner
Art Unit 1634

/Carla Myers/
Primary Examiner, Art Unit 1634